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Cystoid macular edema and use of non-steroidal anti-inflammatory drugs after cataract surgery

Anti-inflamatórios não hormonais e edema macular cistoide no pós-operatório de catarata

Antiinflamatorios no hormonales y edema macular cistoide en el postoperatorio de catarata

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ABSTRACT

Cystoid macular edema (CME) after cataract surgery may compromise visual recovery and worsen the quality of life, thereby preventing early improvement in visual acuity expected after phacoemulsification. The use of non-steroidal anti-inflammatory drugs (NSAIDs) for preventing and treating CME is a controversial topic. With an important review of this topic, the Brazilian Society for Cataract and Refractive Surgery offers the most recent information on the use of NSAIDs and cases of CME in patients who have undergone cataract surgery.

Keywords:
Macular edema;
Tomography, Optical coherence;
Anti-Inflammatory agents;
Visual acuity.

RESUMO

O edema macular cistoide pós-cirurgia de catarata (EMC) pode comprometer a recuperação visual piorando a qualidade de vida dos pacientes e, assim, frustrar a expectativa de melhora precoce da acuidade visual que a facoemulsificação proporciona. A utilização dos anti-inflamatórios não hormonais (AINH) para a prevenção e tratamento do EMC é um tema controverso. A Sociedade Brasileira de Cirurgia Refrativa e Catarata (ABCCR/ BRASCS) com esta importante revisão sobre o tema oferece o que há de mais atual a respeito de AINH e EMC em pacientes submetidos à cirurgia de catarata.

Palavras-Chave:
Edema macular;
Tomografia de coerência óptica;
Anti-Inflamatórios;
Acuidade visual.

RESUMEN

El edema macular cistoide post-cirugía de catarata (EMC) puede comprometer la recuperación visual desmejorando la calidad de vida de los pacientes y, así, hacer fracasar la expectativa de mejora precoz de la acuidad visual que la facoemulsificación proporciona. La utilización de los antiinflamatorios no hormonales (AINH) para la prevención y tratamiento del EMC es un tema polémico. La Sociedad Brasileña de Cirugía Refractiva y Catarata (ABCCR/ BRASCS), con esta importante revisión sobre el tema, ofrece lo que hay de más actual respecto a AINH y EMC en pacientes sometidos a la cirugía de catarata.

Palabras Clave:
Edema macular;
Tomografía de coherencia óptica;
Antiinflamatorios;
Agudeza visual.

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INTRODUCTION

Similar to all surgical procedures, phacoemulsification, although technical and effective, triggers inflammation. Phacoemulsification triggers the release of chemical mediators (such as prostaglandins) from the ciliary body and iris. Uncontrolled postoperative inflammation of the anterior segment is a common complication that compromises the outcome of cataract srugery[1].

Briefly, the trauma of surgery triggers the release of phospholipids from cell membranes. Phospholipase A2 and C enzymes break down these phospholipids into arachidonic acid, which is converted into prostaglandins and thromboxanes by cyclooxygenase enzymes (COX-1 and COX-2) and into leukotrienes by lipoxygenase enzymes. Thus, the trauma induced by phacoemulsification promotes a pro-inflammatory environment: prostaglandins produce vasodilation, stimulate platelet aggregation, and increase the sensitivity of nociceptors (pain), whereas leukotrienes increase vascular permeability and leukocyte chemotaxis, i.e., they create an environment that favors the rupture of the blood–ocular barrier[1].

One consequence of the rupture of the blood–ocular barrier is the increase in the permeability of the retinal pigment epithelium, which facilitates the accumulation of fluid in the ocular tissues, particularly in the perifoveal region. This process may lead to the formation of cystoid macular edema (CME), which has a prevalence rate of 0.1%–2.35% in patients who have undergone phacoemulsification [2].

The pathophysiology of CME is multifactorial. It is attributed to postoperative inflammation alone, as described previously, and is amplified in patients with uveitis, vascular occlusions, epiretinal membranes, and diabetes or by excessive surgical manipulation as well as vitreous loss. One problem associated with postoperative CME is compromised visual recovery and worsened quality of life, which prevents early improvement in visual acuity expected after phacoemulsification.

Non-steroidal anti-inflammatory drugs (NSAIDs) were first described in 1970, and since then, there has been a consensus regarding the importance of these drugs in the regulation of inflammatory events in the human body. They directly inhibit COX-1 and COX-2 enzymes, thereby inhibiting the production of prostaglandins and thromboxanes in cases of inflammation or surgery[1,2,3].

Based on the pathophysiology of the inflammatory process, the use of NSAIDs in the pre- and postoperative periods of cataract surgery has been proposed for preventing the development of CME as well as for facilitating mydriasis and for serving as an analgesic[2,3,4]. This conduct has been adopted by an average of 90% of the cataract surgeons interviewed by the American Society of Cataract and Refractive Surgery [5]. Although the use of NSAIDs appears to prevent the formation of postsurgical CME, it is an additional expense for patients. The sale of NSAIDs for ophthalmology alone is massive in the global NSAID market. Although most ophthalmologists continue using NSAIDs, the association between their use and the prevention of CME is still controversial. Meta-analyses have not provided a consensus on this controversy because immediate postoperative CME is generally self-limiting and resolves spontaneously. Most studies on this subject focus on the immediate postoperative period, in which the course of CME is independent of the use of NSAIDs, and the efficacy of these drugs in the late postoperative period is overlooked. Therefore, many studies that have evaluated this process have tended to maximize the beneficial effects of NSAIDs in the early postoperative period, which has created a bias in the results[5,6,7].

There is subjective evidence that NSAIDs are effective in increasing comfort and decreasing pain after phacoemulsification. Objective studies, such as the one performed by Bucci and Waterbury in 2011, which measured the concentration of prostaglandin (PGE-2) in the anterior chamber of patients who underwent phacoemulsification and were administered three types of NSAIDs in the preoperative period (0.45% ketorolac trometamol, 0.09% bromfenac, and 0.1% nepafenac), have concluded that NSAIDs are effective in reducing PGE-2 levels in the anterior chamber and that ketorolac is the most effective NSAID[3]. In a study performed by Sahu et al [8], which compared the effect of the same NSAIDs (0.4% ketorolac trometamol, 0.1% nepafenac, and 0.09% bromfenac) after phacoemulsification and evaluated their efficacy in reducing anterior chamber flare quantified by laser photometry, the authors have found that all NSAIDs are effective in reducing postoperative inflammation, with a greater reduction in anterior chamber flare observed 4 weeks after surgery with the use of 0.1% nepafenac. However, the efficacy in reducing anterior chamber flare was not associated with a lower incidence of CME after surgery.

The ability of NSAIDs to inhibit prostaglandin concentration in the anterior segment may be very useful in phacoemulsification associated with a femtosecond laser, in which large amounts of prostaglandins are released in the anterior chamber probably due to the action of the laser on the anterior capsule. This explains the immediate miosis observed in patients after they undergo phacoemulsification using a femtosecond laser[9]. Therefore, the preoperative use of NSAIDs may prevent this complication in such patients; however, future

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controlled studies are required to prove this efficacy. The important question is whether the action of NSAIDs on the anterior segment, which reduces the production of prostaglandins, will translate into direct benefits and reduced incidence of postoperative CME.

In 2013, Corrêa et al[10] found that macular thickness always increases after phacoemulsification, i.e., causes edema, as defined exclusively by optical coherence tomography (OCT) measurements. However, this variation in macular volume does not reflect the changes in visual acuity. Tzelikis et al[11] performed a prospective controlled and randomized study to compare 0.4% ketorolac trometamol and 0.1% nepafenac combined with 1.0% prednisolone to placebo as part of a 4-week dose regression system to evaluate the effects of NSAIDs on the prevention of postoperative CME after complication-free phacoemulsification. The incidence of CME was measured as the variation in the macular and foveal thickness using OCT 1, 4, and 12 weeks after surgery. The authors concluded that NSAIDs are not effective in preventing CME after phacoemulsification compared with placebo. In a study published in Ophthalmology in December 2015, Shorstein et al [7] have estimated the rate of CME (visual acuity < 20/40, increase in macular thickness measured by OCT) to be 0.73%, particularly among black patients and patients with comorbidities that predisposed them to CME. They have also reported that the association between NSAIDs and prednisolone acetate reduced the risk of CME by 55% in this specific group.

There is evidence that NSAIDs are effective in preventing clinical CME, but the small number of samples studied hinders the establishment of criteria for the diagnosis of CME and the fact that many of the published studies have been sponsored by the pharmaceutical industry hinders the credibility of the outcomes[7,11]. NSAIDs are an important tool for treatment in ophthalmology. Given the negative impact that clinical CME has in the postoperative period among patients who have undergone phacoemulsification, we must seek options to prevent this complication[2,3,4,5,6,7]. NSAIDs may be useful, but as described previously, credible studies are required to assure physicians that the broad or restrictive prescription of NSAIDs is safe and to justify the additional cost of NSAIDs for these patients in the postoperative period.

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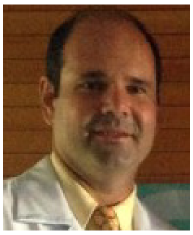
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